IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Ream et al.
Appl. No.: 09/286,818
Conf. No.: 5472
Filed: April 6, 1999
Title: PHARMACEUTICAL CHEWING GUM FORMULATIONS
Art Unit: 1615
Examiner: S. Tran
Docket No.: 112703-035

AFFIDAVIT UNDER 37 C.F.R. § 1.132

Sir:

I, Ronald Ream, hereby state as follows:

1. My experience and qualifications are as follows:
Chemistry B.S. N.I.U. 1964
MBA LOYOLA CHICAGO 1970
Adv. Certificate I.I.T. FOOD SCIENCE 1974
40 YEARS EXP., 30 FOOD & DRUG. PATENTS

2. I am one of the named inventors of the above-identified patent application and am therefore familiar with the inventions disclosed therein.

3. I have reviewed the outstanding Office Action dated July 29, 2005 pending against the above-identified patent application. As one having ordinary skill in the art, I believe that the originally filed specification provides sufficient support for the amended Claims 1, 7 and 19 to apprise the skilled artisan that the inventors, at the time the application was filed, had possession of the claimed subject matter.

4. The claimed invention of the above-identified patent application relates to a method for delivering a medicament to an individual. The method comprises, in part, providing a chewing gum having at least one medicament. The medicament has a uniform distribution

throughout the chewing gum that is less than a typical amount of medicament that is swallowed by the individual to achieve a bioequivalent effect. The gum is chewed to cause the medicament to be released from the chewing gum composition into the buccal cavity of the individual. The continued chewing of the gum thereby creates a fluid pressure causing the medicament to enter the systemic system of the individual through an oral mucosa of the individual.

5. Typically, drugs or medicaments are administered parenterally or enterally. Parenteral administration is the administration of a drug intravenously directly into the blood stream. Enteral refers to the administration of a drug into the gastrointestinal tract. In either case, the goal of the drug administration is to move the drug from the site of administration towards the systemic circulation. In determining the efficacy of a drug and the effectiveness of the use of a drug to treat a disease, drug absorption is a critical concern. Drug absorption refers to the process of drug movement from the site of administration toward the systemic circulation.

6. Oral administration of drugs is by far the most common method. When administered orally, the drugs are typically ingested or swallowed, and drug absorption usually occurs due to the transport of cells across the membranes of the epithelial cells within the gastrointestinal tract. A further issue effecting the absorption of orally administered drugs is the form of the drug. Most orally administered drugs are in the form of tablets or capsules. These capsules or tablets must be disintegrated or dissolved before absorption can occur. There are a variety of factors capable of varying or retarding disintegration of solid dosage forms. Further, there are a variety of factors that effect the dissolution rate and therefore determine the availability of the drug for absorption.

7. Not only is drug absorption an issue in drug delivery, but, also the bioavailability of the drug is also critical. Bioavailability is defined as the rate at which and the extent to which the active moiety (drug or metabolite) enters the general circulation, thereby gaining access to the site of action. Bioavailability depends upon a number of factors, including how a drug product is designed and manufactured, its physicochemical properties and factors that relate to the physiology and pathology of the patient.

8. When a drug rapidly dissolves from a drug product and readily passes across membranes, absorption from most site administration tends to be complete. This is not always the case for drugs given orally. Before reaching the vena cava, the drug must move down the alimentary cannel and pass through the gut wall and liver, which are common sites of drug metabolism. Thus, the drug may be metabolized before it can be measured in the general circulation. This causes a decrease in drug input that is called the first pass effect. A large number of drugs show low bioavailability owing to an extensive first pass metabolism.

9. The present invention provides improved methods for delivering medicaments and other agents to an individual as well as improved chewing gum formulations including such medicaments and agents. Pursuant to the present invention, a medicament or agent is contained in a chewing gum formulation. Accordingly, as the chewing gum is chewed, the medicament or agent is released into the saliva. In contrast to a typically orally ingested drug, wherein the solution is in contact too briefly for absorption to be appreciable through the oral mucosa, it is believed that during chewing the medicament or agent in the saliva is forced through the oral mucosa in the buccal cavity due to the pressure created by the chewing. The oral mucosa has a thin epithelium and a rich vascularity. Thus, the oral mucosa favors drug absorption.

10. Applicants have surprisingly found that an increase in the absorption of the drug is achieved via chewing gum as well as an increase in the bioavailability of the drug as compared to typical enteral or oral administration. Applicants have also found that less medicament or agent can be placed in the chewing gum than is typically enterally or orally administered to an individual to achieve an effect and the same bioequivalents can be achieved. Consequently, a smaller or reduced amount of medicament or agent is needed in the chewing gum to achieve the same bioavailability or bioequivalent effect in the body of the consumer as a larger amount of the same medicament or agent that is typically swallowed by the consumer.

11. Applicants have provided examples that show actual reduction to practice of the claimed subject matter. For example, the caffeine study of Experiment 2 demonstrates that the

administration of the medicament or agent via a chewing gum through the buccal cavity can provide an increased effect than when the same medicament or agent is taken through enteral or oral administration. The study compares the bioequivalent effect/bioavailability of caffeine in consumers' bloodstream after chewing caffeine containing gum versus swallowing caffeine pills. These examples demonstrate that less caffeine can be provided in the claimed product than that that is typically ingested, for example, through No Doze, and still achieve as good if not greater effect on a consumer. Experiment 4 demonstrates that the chewing gum agents are indeed adsorbed in the oral cavity.

12. For all the foregoing reasons, as one having ordinary skill in the art, I believe that Applicants' originally filed specification provides support for the method of delivering a medicament to an individual by providing a chewing gum having a uniform distribution of a medicament throughout the chewing gum that is less than a typical amount of medicament that is swallowed by the individual to achieve a bioequivalent effect. The gum is chewed to cause the medicament to be released from the chewing gum composition into the buccal cavity of the individual and the medicament enters the systemic system of the individual through an oral mucosa of the individual. Accordingly, the specification reasonably conveys to one having ordinary skill in the art that Applicants had possession of the claimed invention at the time of filing the present application.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, Title 18, United States Code, and that willful false statements may jeopardize the validity of this patent and any patent issuing therefrom.

Date: 10/17/05

RS Ream

Name: Ronald Ream